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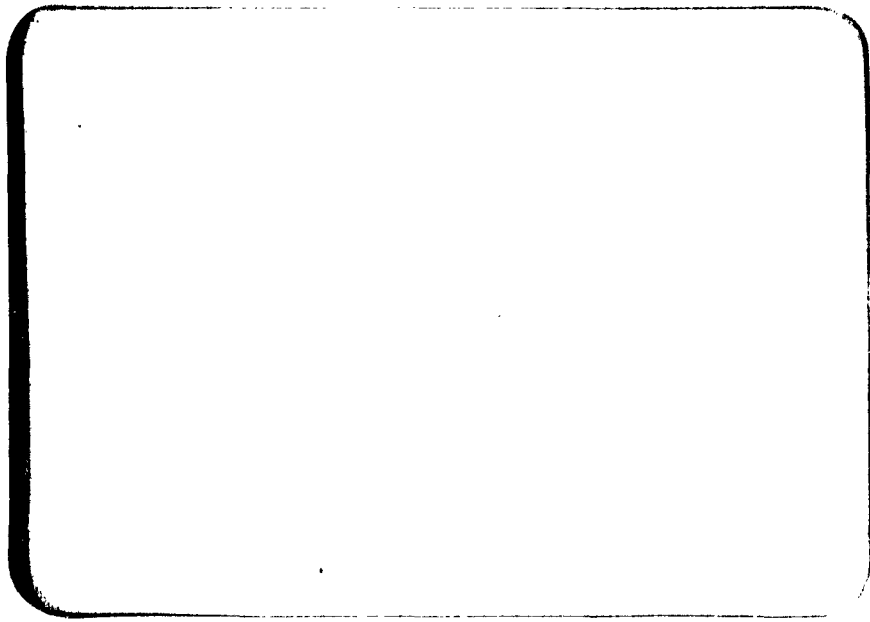


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ABSTRACT

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Accession No. _____

Chemicals and Plastics Division
Food Machinery and Chemical Corporation
Baltimore, Maryland

Synthesis of Compounds for Use in Chemical Warfare Research
G. Sumrell

Bimonthly Report No. 13, March-April, 1961. pp. 7
plus Synthesis Reports

Contract No. DA18-108-405-CML-296
Contract No. DA18-108-CML-6572
Project No. 4-08-03-016-07, X.O.5-455-01 (R and D), CC511
Project No. 4-08-03-016-07, X.O.5-408-01, CC511

Classification: Unclassified

A method is reported for the synthesis of each of the following eight compounds.

2-Dimethylaminobenzaldehyde

3-Dimethylaminobenzaldehyde

1-(2',2'-Diphenyl-2'-hydroxyethyl)-4-methylpiperazine Dihydrochloride

3- β -Hydroxyethyl-4-methyl-5-phenyloxazolidine Hydrochloride

2-Hydroxymethyl-1-cyclohexanone

4-Nitro-7,8,9,10-tetrahydrophenanthridine

2-(4'-Phenylpiperidino)-ethanol

1-(4'-Pyridyl)-2-nitro-2-phenylethanol

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Summary

A procedure for each of the following syntheses is given:

2-Dimethylaminobenzaldehyde

3-Dimethylaminobenzaldehyde

1-(2',2'-Diphenyl-2'-hydroxyethyl)-4-methylpiperazine Dihydrochloride

3- β -Hydroxyethyl-4-methyl-5-phenyloxazolidone Hydrochloride

2-Hydroxymethyl-1-cyclohexanone

4-Nitro-7,8,9,10-tetrahydrophenanthridine

2'-(4'-Phenylpiperidino)-ethanol

1-(4'-Pyridyl)-2-nitro-2-phenylethanol

Experimental

Procedures are given for the synthesis of eight compounds in the appended Synthesis Reports Nos. 109 to 116 inclusive.

The attached tabulations show the following information:

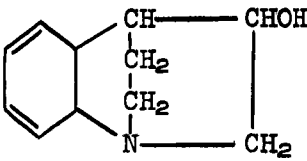
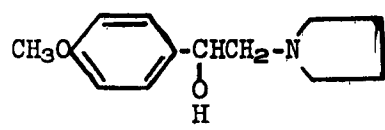
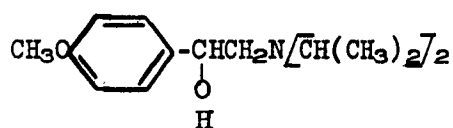
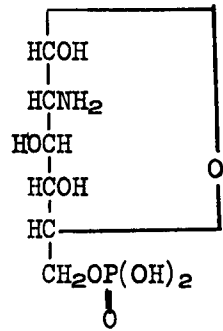
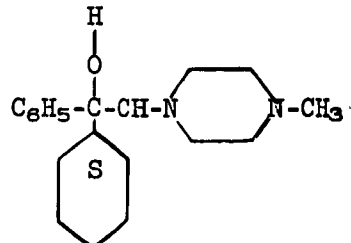
Table I. A summary of all compounds which were worked on in the laboratory during the report period. Compounds are listed both by code numbers and by formulas.

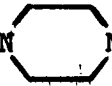
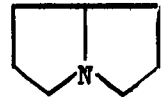

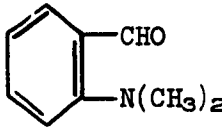
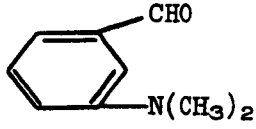
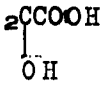
Table II. Compounds which have been added to the list during this report period, but on which no laboratory work has been done are listed by code numbers only.

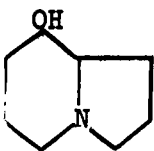
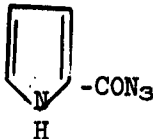
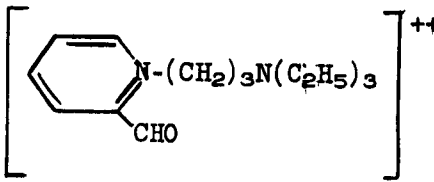
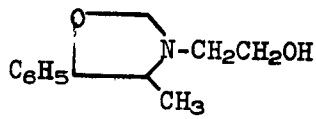
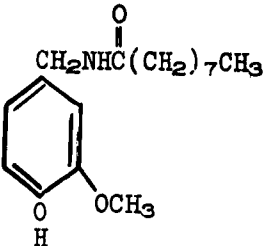
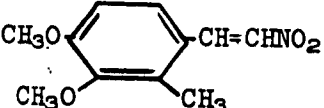
Table III. Compounds which have been cancelled or deferred during this report period are listed by code numbers only.

Table IV. Compounds on which no laboratory work has been done, but which are still active are listed by code number only.

Table I

<u>Compound No.</u>	<u>Formula</u>	<u>Status</u>
(U)M-304		Cancelled by letter: March 27, 1961. Expenditure: \$1225.00.
(U)M-400		Cancelled by letter: March 27, 1961. Expenditure: \$1125.00.
(U)M-401		Cancelled by letter: March 27, 1961. Expenditure: \$1000.00.
(U)SX-412		In process. Expenditure to date: \$650.00
(U)M-414		In process. Expenditure to date: \$1100.00

<u>Compound Code No.</u>	<u>Formula</u>	<u>Status</u>
(U)M-415	$(C_6H_5)_2C(OH)CH_2-N$  $N-CH_3$	Delivered March 10, 1961. Expenditure: \$825.00
(U)M-431	 OH	In process. Expenditure to date: \$450.00
(U)M-433	 $-CH(OH)CH(NO_2)C_6H_5$	Delivered March 10, 1961. Expenditure: \$75.00
(U)S-445		One sample delivered April 25, 1961. Expenditure to date: \$700.00.
(U)S-446		One sample delivered March 29, 1961. Expenditure to date: \$2625.00
(U)S-449	$(p-C_6H_5-C_6H_4)_2$ 	In process. Expenditure to date: \$1000.00
(C)M-452	See Second Annual Report, Volume III for formula	In process. Expenditure to date: \$800.00.

<u>Compound Code No.</u>	<u>Formula.</u>	<u>Status</u>
(U)M-457		Cancelled by letter March 27, 1961. Expenditure: \$100.00.
(U)SX-460		In process. Expenditure to date: \$75.00
(U)S-465		2 Br ⁻ In process. Expenditure to date: \$975.00
(U)M-472		Delivered March 10, 1961 Expenditure: \$350.00
(U)M-473		In process. Expenditure to date: \$775.00
(U)M-476		In process. Expenditure to date: \$500.00.

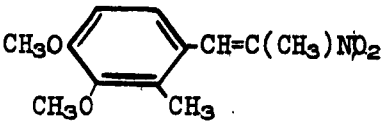
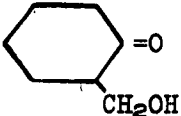
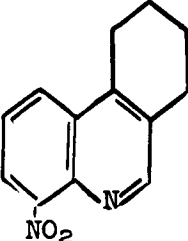
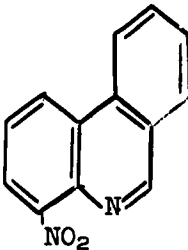
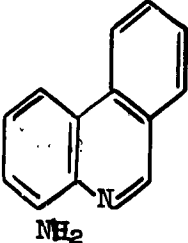
<u>Compound No.</u>	<u>Formula</u>	<u>Status</u>
(U)M-477		<p>In process.</p> <p>Expenditure to date: \$500.</p>
(U)SX-480		<p>Delivered April 12, 1961</p> <p>Expenditure: \$375.00</p>
(U)SX-481		<p>Delivered April 25, 1961</p> <p>Expenditure: \$375.00</p>
(U)SX-482		<p>In process.</p> <p>Expenditure to date: \$425.00</p>
(U)SX-483		<p>In process.</p> <p>Expenditure to date: \$425.00</p>

Table II

(U)M-486	(U)M-487
(U)M-488	(U)M-489

Table III

(U)M-304	(U)M-400	(U)M-401
(U)M-457	(U)S-463	(U)S-474
(U)M-475	(U)M-488	(U)M-489

Table IV

(U)M-458
(U)M-478
(U)M-479
(U)M-486
(U)M-487

Chemicals and Plastics Division
Food Machinery and Chemical Corporation
Baltimore, Maryland

Synthesis Report No. 109

Contract No. DA18-108-405-CML-296

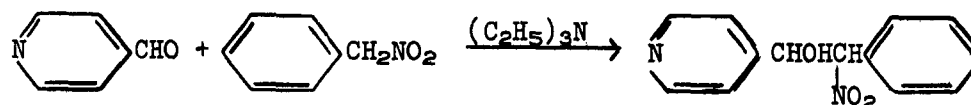
Contract No. DA18-108-CML-6572

Compound Code No. (U)M-433

February 24, 1961

The Preparation of 1-(4'-Pyridyl)-2-nitro-2-phenylethanol¹

Reaction:



Procedure:

A solution of 51.2 g. (0.374 mole) of phenylnitromethane, 40.1 g. (0.374 mole) of pyridine-4-carboxaldehyde, and a few drops of triethylamine in 90 ml. of anhydrous ethanol stood over the weekend at room temperature. The hard crystals which formed were separated by filtration, slurried with enough ethanol to cover them and again separated by filtration. After two washes with about 10 ml. of ethanol, the crystals were dried in a vacuum oven at room temperature. The 1-(4'-pyridyl)-2-nitro-2-phenylethanol, 54.3 g. (60 percent of the theoretical yield), was obtained as creamy-white crystals which melted at 134-135°C. with decomposition (literature¹, m.p. 130-130.5 with decomposition).

Reference:

1. Robertson, D. N., J. Org. Chem., 25, 374 (1960).

Characterization:

C₁₃H₁₂N₂O₃; m.w. 244.25; 53.9 g.; m.p. 134-135°C. with decomposition (literature¹, 130-130.5°C. with decomposition).

Compound Code No. (U)M-433

-2-

February 24, 1961

Time (Man-days):

	<u>Ph.D. Chemist</u>	<u>B.S. Chemist</u>	<u>Technician</u>
Literature	---	---	---
Synthesis	---	1 1/4	---
Analysis	---	---	---

Estimated Expenditure:

\$75.00


R. A. Meara

RAM/mpi
2/24/61

Chemicals and Plastics Division
Food Machinery and Chemical Corporation
Baltimore, Maryland

Synthesis Report No. 110

Contract No. DA18-108-405-CML-296

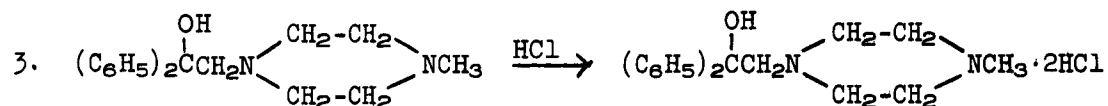
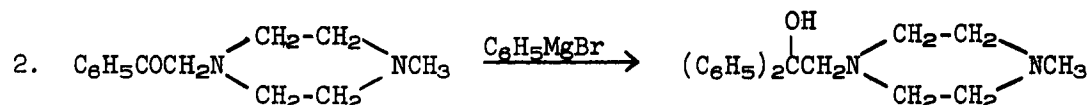
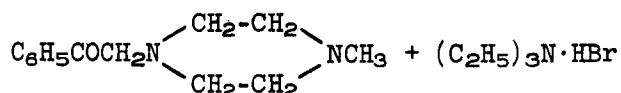
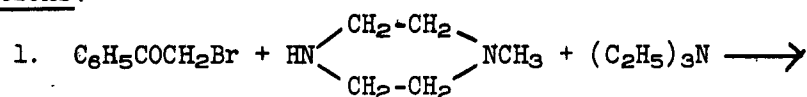
Contract No. DA18-108-CML-6572

Compound Code No. (U)M-415

March 7, 1961

The Preparation of 1-(2',2'-Diphenyl-2'-hydroxyethyl)-
4-methylpiperazine Dihydrochloride

Reactions:



Procedure:

The Preparation of 1-Methyl-4-phenacylpiperazine.

A solution of 95.6 g. (0.48 mole) of phenacyl bromide in 140 ml. of anhydrous xylene was added over a period of two hours to a stirred solution of 57.6 g. (0.57 mole) of 1-methylpiperazine and 58.2 g. (0.57 mole) of triethylamine in 140 ml. of anhydrous xylene heated on the steam bath. After the addition was complete, the mixture was stirred and refluxed for 16 hours. The reaction mixture was cooled and filtered to remove the triethylamine hydrobromide. The filtrate was extracted three times with dilute hydrochloric acid. The aqueous portion,

which contained solid, was stirred and cooled while 50 percent sodium hydroxide solution diluted with an equal quantity of ice was added until the mixture was strongly alkaline. The resulting solid was extracted with a 1:1 mixture of ether and benzene. This solution was dried with MgSO_4 and the solvent was removed under vacuum. The residual material was distilled through a 1-foot Vigreux column and an air condenser to yield 65.6 g. (62.5 percent of the theoretical yield) of 1-methyl-4-phenacylpiperazine which boiled at 122-123.5°C. at 0.7 mm. pressure. Thirty-six grams of this material, which melted at 58-61°C. (the literature¹ gives 60-62°C.) was used in the next step.

The Preparation of 1-(2',2'-Diphenyl-2'-hydroxyethyl)-4-methylpiperazine.

A solution of 36.0 g. (0.17 mole) of 1-methyl-4-phenacylpiperazine in 360 ml. of anhydrous toluene was added slowly to a stirred cooled solution of phenylmagnesium bromide prepared from 7.3 g. (0.30 mole) of magnesium and 47.4 g. (0.30 mole) of bromobenzene in 250 ml. of anhydrous ether. The ether was removed by distillation and the toluene suspension was stirred and refluxed for three hours. After cooling, the reaction mixture was treated dropwise with a solution of 30 g. of ammonium chloride in 120 ml. of water. An emulsion which formed was broken with the addition of more water. The toluene layer was separated, the aqueous layer was extracted twice with ether, and the combined organic extracts were dried with MgSO_4 and concentrated under vacuum. The residue was distilled to yield 16.5 g. (32.6% of the theoretical yield) of 1-(2',2'-diphenyl-2'-hydroxyethyl)-4-methylpiperazine which boiled at 160-165°C. at 0.2 mm. pressure, n_D^{25} 1.5740 (the literature¹ gives n_D^{25} 1.5727 for crude material).

The Preparation of 1-(2',2'-Diphenyl-2'-hydroxyethyl)-4-methylpiperazine Dihydrochloride.

A solution of 16.5 g. (0.06 mole) of 1-(2',2'-diphenyl-2'-hydroxyethyl)-4-methylpiperazine in 50 ml. of anhydrous ethanol was added with stirring to a

March 7, 1961

cooled solution of 5.2 g. (0.14 mole) of anhydrous hydrogen chloride in 100 ml. of anhydrous ethanol. The solid which formed was filtered, washed with cold ethanol and vacuum dried. The dry 1-(2',2'-diphenyl-2'-hydroxyethyl)-4-methyl-piperazine dihydrochloride weighed 17.0 g. (77.0% of the theoretical yield), melted at 220.5-222.0°C. (the literature¹ gives a melting point of 224-225°C.) and contained 18.96% ionizable chlorine (calculated ionizable chlorine, 18.97%).

Reference:

1. Zaugg, H. E., et al., J. Am. Chem. Soc., 80, 2765-2766 (1958).

Characterization:

C₁₉H₂₆N₂OCl₂; m.w. 369.33; 16.6 g.; m.p. 220.5-222.0°C. (literature¹, m.p. 224-225°C.); analysis; chlorine: calculated 18.97%, found 18.96%.

Time (Man-days):

	<u>Ph.D. Chemist</u>	<u>B.S. Chemist</u>	<u>Technician</u>
Literature	---	1/2	---
Synthesis	---	10 3/4	---
Analysis	---	---	---

Estimated Expenditure:

\$825.00

W. P. Brian
W. P. Brian

WPB/mpl

Chemicals and Plastics Division
Food Machinery and Chemical Corporation
Baltimore, Maryland

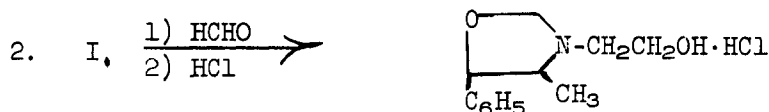
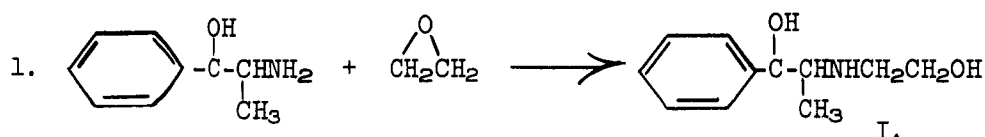
Synthesis Report No. 111
Contract No. DA18-108-405-CML-296
Contract No. DA18-108-CML-6572

Compound Code No. (U)M-472

March 6, 1961

The Preparation of 3-β-Hydroxyethyl-4-methyl-5-phenyloxazolidine Hydrochloride

Reactions:



Procedure:

The Preparation of N-β-Hydroxyethylnorephedrine¹.

A solution of 29.3 g. (0.194 mole) of norephedrine and 9.5 g. (0.216 mole) of ethylene oxide in 200 ml. of anhydrous ethanol was placed in a hydrogenation bomb and was heated at 55 to 68°C. with stirring for 21 hours. The solvent was removed at reduced pressure and the residue triturated with anhydrous ether. The resultant solid was separated by filtration, washed twice with ether and dried. The N-β-hydroxyethylnorephedrine, 16.8 g. (44% of the theoretical yield), was obtained as a white, crystalline solid which melted at 108°C. (literature, 110-111.5°C.¹ and 109°C.²).

The Preparation of 3-β-Hydroxyethyl-4-methyl-5-phenyloxazolidine Hydrochloride.¹

To a suspension of 16.8 g. (0.086 mole) of N-β-hydroxyethylnorephedrine in 45 ml. of water was added 9.0 g. (0.10 mole) of 36% aqueous formaldehyde and the mixture, in a separatory funnel, was shaken vigorously for 10 minutes. The mixture was extracted with two 100 ml. portions of chloroform. The extracts were

March 6, 1961

dried over anhydrous magnesium sulfate, filtered, and the solvent removed under vacuum. The yellow oil which remained was dissolved in 150 ml. of anhydrous ethanol and into this solution hydrogen chloride was bubbled. Ether was added until turbidity and then the crude organic salt crystallized. It was recrystallized from anhydrous ethanol and ether. The 3- β -hydroxyethyl-4-methyl-5-phenyl-oxazolidine, 10.5 g. (50% of the theoretical yield), was obtained as a white crystalline solid, m.p. 104-105°C. (literature¹, m.p. 107-110°C.). By analysis, 14.48% chlorine was found (literature¹, found, 14.40% Cl); 14.55% chlorine was calculated.

Reference:

1. Kalm, M. J., J. Org. Chem., 25, 1934 (1960).
2. Skita, A. and Keil, F., Ber. 63B, 34 (1930).

Characteristics:

C₁₂H₁₈ClNO₂; m.w. 243.73; 10.2 g.; m.p. 104-105°C. (literature¹, m.p. 107-110°C.); Analysis: chlorine; calculated, 14.55%; found, 14.48% (literature¹, 14.40%).

Time (Man-days):

	<u>Ph.D. Chemist</u>	<u>B.S. Chemist</u>	<u>Technician</u>
Literature	---	1/4	---
Synthesis	---	5	---
Analysis	---	---	---

Estimated Expenditure:

\$350.00


R. A. Meara

RAM/impl
3/6/61

gave 137 g. (62% of the theoretical yield) of dimethyl sulfite at 124-126°C., n_D^{25} 1.4070 (literature², b.p. 126°C., n_D^{20} 1.4093).

The Preparation of 3-Nitrobenzaldehyde Dimethylacetal¹

To a 500-ml. 3-necked flask fitted with a thermometer and reflux condenser was added 113 g. (0.75 mole) of 3-nitrobenzaldehyde, 91 g. (0.825 mole) of dimethyl sulfite, and 90 ml. of methanol. Dry hydrogen chloride was passed into the flask for a few minutes. The mixture was stirred by means of a magnetic stirrer and was slowly warmed to the boiling point and refluxed overnight. It was then allowed to cool and was poured into 280 ml. of ice-cold 20% sodium hydroxide solution contained in a 2-l. beaker. This mixture was stirred for 3 hours, followed by the addition of 800 ml. of water. The mixture was extracted two times in series with 300-ml. portions of ether and the extracts washed in series with 100 ml. portions of water until neutral. They were then combined and dried over magnesium sulfate. Fractionation gave 141 g. (95% of the theoretical yield) of product at 98-100°C./1 mm., n_D^{25} 1.5220 (literature³, b.p. 141-143°C./8 mm.).

Reduction and Methylation

A sample of 125 g. (0.63 mole) of the dimethyl acetal of 3-nitrobenzaldehyde was reduced, and the resulting amine methylated in the following manner: In a 3-l. 3-necked flask fitted with a mechanical stirrer, thermometer, dropping funnel and reflux condenser was placed 1210 g. (5.04 moles^d) of sodium sulfide nonahydrate. This material was warmed until it melted (about 50°C.) and then 333 ml. (4 moles) of concentrated hydrochloric acid was slowly added with mild cooling to keep the temperature below 70°C., followed by the addition of the acetal in one portion. The mixture was stirred until the mildly exothermic part of the reaction was over (about one-half hour), and then was heated under reflux for 8 hours.^a The mixture was then allowed to cool and was extracted two times in series with 300-ml. portions of ether. The ether extracts were washed in series

March 21, 1961

polymerization of the aminoaldehyde and a substantial reduction in the yield of final product. On an earlier run (see reference 4) it was found that an 8-hour reflux period was ample for complete reduction and gave very little polymerization of the product.

b) The literature¹ indicates that the acetal of 3-aminobenzaldehyde is present at this point, though the compound was not isolated. In our work, an attempt to isolate this acetal resulted in polymerization of the aminoaldehyde, indicating that hydrolysis of the acetal had occurred even in the basic reaction mixture (see reference 4).

c) This methylation proved to be very slow and hard to take to completion. When the methylation was incomplete, the product was primarily in the ether layer as the monomethylated intermediate at this point.

References:

1. Cocker, W., et al., J. Chem. Soc., 751 (1938).
2. Vogel, A. I., and Cowan, D. M., J. Chem. Soc., 22 (1943).
3. Inke, R. N., et al., Org. Synth., Coll. Vol. III, 644 (1955).
4. Synthesis Report No. 99, dated January 12, 1961, Contract No. DA18-108-405-CML-296, DA18-108-CML-6572, Compound Code No. (U)S-444.

Characterization:

C₉H₁₁NO; m.w. 149.19; 19 g.; b.p. 134-135°C./12 mm.; n_D²⁵ 1.5675 (literature,¹ b.p. 112°C./7 mm.).

Time (man-days):

	<u>Ph.D. Chemist</u>	<u>B.S. Chemist</u>	<u>Technician</u>
Literature	1	---	---
Synthesis	7	---	35
Analysis	---	---	---

Estimated Expenditure:

\$2350.00

GS/mpi
3/28/61

G. Sumrell
G. Sumrell (G.A.M.)

Chemicals and Plastics Division
Food Machinery and Chemical Corporation
Baltimore, Maryland

Synthesis Report No. 113

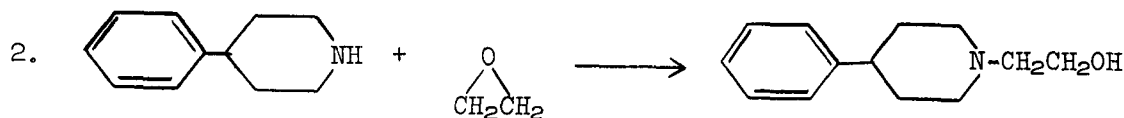
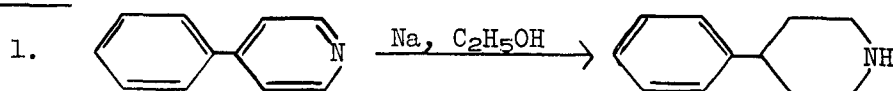
Contract No. DA18-108-405-CML-296
Contract No. DA18-108-CML-6572

Compound Code No. (U)M-468

March 22, 1961

The Preparation of 2-(4'-Phenylpiperidino) ethanol¹

Reactions:



Procedure:

The Preparation of Phenylpiperidine.²

To a solution of 27.8 g. (0.18 mole) of phenylpyridine in a liter of anhydrous ethanol was added 70.0 g. (3.05 atoms) of sodium. The metal, in pieces as large as could be put through the neck of the 3-l. reaction flask, was added portionwise at a rate which prevented the reaction from becoming too vigorous. However, it was necessary to heat the solution to reflux towards the end and this was continued for two hours after the sodium had dissolved. After cooling, 500 ml. of water (the first 50 ml. portion added dropwise) was added while stirring and the alcohol was then removed under vacuum until two phases started to distill. The mixture was cooled and the organic phase separated; the aqueous phase was extracted once with an equal volume of ether. The organic material was combined, dried over anhydrous magnesium sulfate, and the solvents removed under vacuum. The burgundy colored residue was then distilled through a

March 22, 1961

one-foot, vacuum-jacketed Vigreux column at reduced pressure but no pure cut was obtained. The phenylpiperidine was obtained as a liquid, 23.2 g., most of which distilled at 73-75°C. at 0.13-0.15 mm. although the range was 68-77°C. at 0.11-0.15 mm.

The Preparation of 2-(4'-Phenylpiperidino)ethanol.¹

The phenylpiperidine, 23.2 g. (0.14 mole), was dissolved in 80 ml. of anhydrous methanol and into the refluxing solution was bubbled 10.0 g. (0.23 mole) of ethylene oxide during 1 1/2 hours. When the addition was complete, the solution was refluxed two hours longer. The solvent and excess ethylene oxide were removed under vacuum and the residue distilled through a one-foot, vacuum-jacketed Vigreux column. The 2-(4'-phenylpiperidino) ethanol distilled at 99-106°C. at 0.2 mm. and 22.6 g. (76% of the theoretical yield) was obtained as a straw-colored liquid, n_D^{24} 1.5442 (literature¹, b.p.o. 1104-108°C., n_D^{24} 1.5442).

References:

1. Nelson, J. L. and Musker, W. K., J. Am. Chem. Soc., 82 5155 (1960).
2. Marvel, C. S. and Lazier, W. A., Organic Syntheses, Collective Volume I, p. 99, 2nd edition, 1941, John Wiley and Sons.

Characterization:

$C_{13}H_{19}NO$; m.w. 205.29; 22.0 g.; b.p.o. 299-106°C., n_D^{24} 1.5442 (literature¹, b.p. o. 1104-108°C., n_D^{24} 1.5442).

Time (Man-days):

	<u>Ph.D. Chemist</u>	<u>B.S. Chemist</u>	<u>Technician</u>
Literature	---	1/4	---
Synthesis	---	5	---
Analysis	---	---	---

Estimated Expenditure:

\$375.00.


R. A. Meera

April 6, 1961

References:

1. Mannich, C. and Brose, W., Ber., 56, 841 (1923).
2. Kenner, J., Ritchie, W. H., and Statham, F. S., J. Chem. Soc., 1170 (1937).

Characterization:

$C_7H_{12}O_2$; m.w. 128.17; 98.0 g.; b.p. 102-103°C. (literature¹, b.p. 114-115°C.); n_D^{25} 1.4777.

Time (Man-days):

	<u>Ph.D. Chemist</u>	<u>B.S. Chemist</u>	<u>Technician</u>
Literature	1/4	1/2	---
Synthesis	---	4 1/4	---
Analysis	---	---	---

Estimated Expenditure:

\$375.00.

W. P. Brian
W. P. Brian

WPB/mdl
4/10/61

Chemicals and Plastics Division
Food Machinery and Chemical Corporation
Baltimore, Maryland

Synthesis Report No. 115

Contract No. DA18-108-405-CML-296

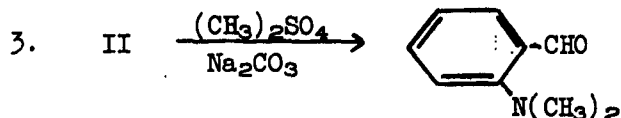
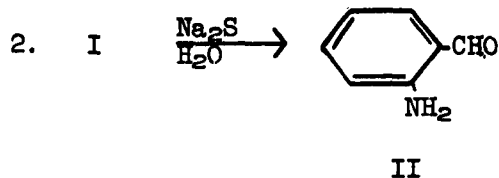
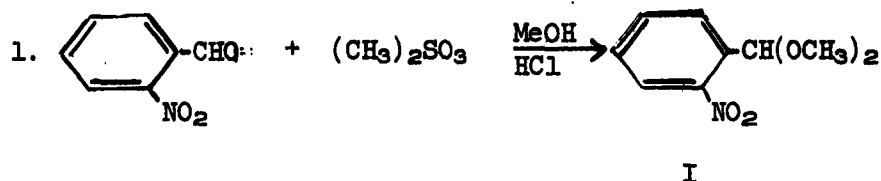
Contract No. DA18-108-CML-6572

Compound Code No. (U) S-445

April 24, 1961

The Preparation of 2-Dimethylaminobenzaldehyde^{1,2}

Reactions:



Procedure:

2-Nitrobenzaldehyde dimethylacetal was prepared in a similar manner to that previously described¹ for the meta-isomer. From 101.5 g. (0.67 mole) of the aldehyde and 83 g. (0.75 mole) of dimethyl sulfite was obtained 129.5 g. (98 percent of the theoretical yield) of acetal distilling at 86-88°C. (1 mm.), n_D^{25} 1.5158.

The acetal (129 g., 0.65 mole) was reduced in the manner described¹ for the meta-isomer using 1200 g. (5 moles) of sodium sulfide nonahydrate and 333 ml.

(4 moles) of concentrated hydrochloric acid. The reaction mixture was refluxed for six hours and left stirring overnight. The product was extracted into ether and methylated (without isolation) in the following manner:

The ether solution (total volume, about 600 ml.) was dried briefly over magnesium sulfate and filtered through a cotton plug into a 5-l., 3-necked flask fitted with a stirrer, thermometer and dropping funnel. To the solution was added 350 g. (3.3 moles) of anhydrous sodium carbonate, followed by the dropwise addition with stirring of 165 g. (1.31 moles) of dimethyl sulfate. No cooling was required for the mildly exothermic addition. The mixture was stirred overnight. Then 86 g. (0.68 mole) more dimethyl sulfate was added and stirring was continued for eight hours, at which point 2500 ml. of water was added in one portion and the mixture left stirring overnight. The next morning 26 g. (0.21 mole) more dimethyl sulfate was added, followed by two more similar additions at 4-hour intervals, and the mixture was left stirring overnight. Then the two layers were separated and the aqueous layer extracted with 300 ml. of ether. The two ether extracts were washed in series with 100 ml. of water and dried over magnesium sulfate. Removal of the solvent left 69 g. of yellow residue^a. Fraction of this material gave a trace of forerun followed by 38.5 g. (40 percent of the theoretical yield) of 2-dimethylamino-benzaldehyde distilling at 121-122°C./13 mm., n_D^{25} 1.5092 (literature², b.p. 120°C./11 mm.).

Note:

a) The product was found in the ether layer at this point, in contrast to the meta-isomer being present in the aqueous layer as the quaternary salt (see reference 1).

References:

1. Synthesis Report No. 112, dated March 21, 1961, Contract No. DA18-108-405-CML-296, DA18-108-CML-6572, Compound Code No. (U)S-446.

April 24, 1961

2. Beil., 14, 25 (1931).Characterization:

$C_9H_{11}NO$; m.w. 149.19 ; 38 g.; b.p. 121-122°C./13 mm.; n_D^{25} 1.5092
(literature², 120°C./11 mm.).

Time (Man-Days):

	<u>Ph.D. Chemist</u>	<u>B.S. Chemist</u>	<u>Technician</u>
Literature	1	---	---
Synthesis	4	---	5
Analysis	---	---	---

Estimated Expenditure:

\$700.00

Gene Sumrell
Gene Sumrell

GS/mpm
4/24/61

Chemicals and Plastics Division
Food Machinery and Chemical Corporation
Baltimore, Maryland

Synthesis Report No. 116

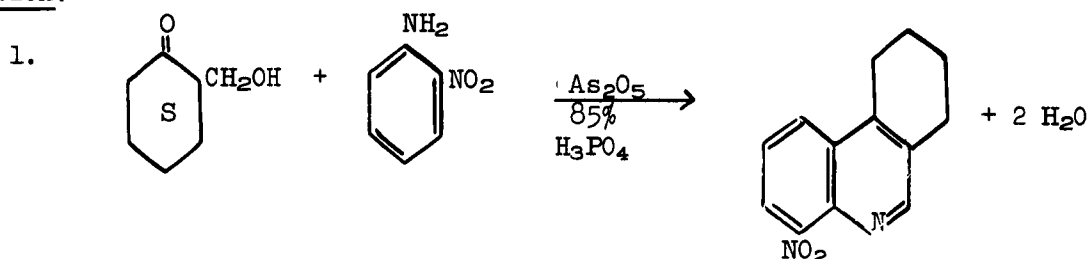
Contract No. DA18-108-405-CML-296
Contract No. DA18-108-CML-6572

Compound Code No. (U)SX-481

April 24, 1961

The Preparation of 4-Nitro-7,8,9,10-tetrahydrophenanthridine¹

Reaction:



Procedure:

A mixture of 69.0 g. (0.50 mole) of o-nitroaniline, 120.0 g. (0.52 mole) of arsenic acid and 500 ml. of 85 percent phosphoric acid was stirred and heated to 100°C. To this was added dropwise 128.0 g. (1.0 mole) of 2-hydroxymethyl-1-cyclohexanone, keeping the temperature below 120°C. When the addition was complete, the reaction mixture was stirred at 118°-120°C. for two hours. It was then poured into ice-water, neutralized with potassium hydroxide solution and filtered. The solid was extracted twice with hot benzene and filtered. The organic layer was separated from the water and concentrated under vacuum to a thick slurry. The residue was filtered and the solid was washed with cold benzene and dried. This first crop weighed 18.2 g. and melted at 140-144°C. The filtrate yielded an additional 7.1 g. of solid. Five grams of the first crop was again washed with benzene to yield 4.0 g. of 4-nitro-7,8,9,10-tetrahydrophenanthridine which melted at 142-144°C. (The literature gives 143-144°C.) This material is being supplied as (U)SX-481. The remaining material will be used in the preparation of (U)SX-482.

April 24, 1961

Reference:

1. Case, F. H., J. Org. Chem. 21, 1070 (1956).

Characterization:

$C_{13}H_{12}N_2O_2$; m.w. 228.25; 4.0 g.; m.p. 142° - $144^{\circ}C$. (literature¹, m.p. 143 - $144^{\circ}C$.).

Time (Man-days):

	<u>Ph.D. Chemist</u>	<u>B.S. Chemist</u>	<u>Technician</u>
Literature	1/4	1/2	---
Synthesis	---	4 1/4	---
Analysis	---	---	---

Estimated Expenditure:

\$375.00

W. P. Brian
W. P. Brian

WPB/impl
4/24/61